III. Remarks

A. Status of the Application

Claims 35-37 are amended. Claims 8-11 and 35-37 are pending.

In the amended claims, the phrase "in all of said labeled substances of the carrier particle" is inserted based on the description, page 5, line 5, and original claim 1 "in all of said labeled substances."

B. Rejections of Claims 8-11 and 35-37 under 35 U.S.C. §112, First Paragraph

Office Action

Claims 8-11 and 35-37 were rejected in the Office Action for failing to comply with the written description requirement. Attention was directed to the decision in *University of Rochester v. G.D. Searle & Co.* 68 USPQ2D 1424 (Fed. Cir. 2004) at 1428. The cited paragraph of the Office Action ends with a quote from *Lockwood*, 107 F.3d at 1572, "Thus, an applicant complies with the written-description requirement by describing the invention, with all its claimed limitations, not that which makes it obvious, and by using such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention."

At item 11. of page 6, the Office Action states a lack of written description of an embodiment where a nucleic acid has a length of 30,303 bases.

At item 12. of page 7, the Office Action states a failure of the disclosure to provide a sequence listing of any nucleic acid.

At item 13. of page 7, the Office Action states a failure of the disclosure to set forth any nucleic acids of a predetermined sequence and labeled with different labels in a "predetermined molar ratio."

Response

The claims have been amended to remove the terms related to "predetermined base sequence" and to "a base sequence." The present invention does not require knowledge of the base sequence of a nucleic acid that is an element of the claimed labeled complexes.

The presently claimed invention relates to properties common to nucleic acids in general. For example, nucleic acids have 3' and 5' ends, they contain sugars and phosphate bonds. Nucleic acids hybridize to their complementary strand by well known rules. Nucleic acids bind proteins that have binding specificity for a particular sequence of the nucleic acid under conditions readily determined by one of skill in the art. The present invention provides a labeled complex that includes nucleic acids and relies on those general properties of nucleic acids that are common to nucleic acids. A requirement for a specific sequence, a specific genus or a specific species of nucleic acid is simply not applicable to the present invention.

Please note that the Court of Appeals for the Federal Circuit stated in *In re Wallach*, 71 USPQ2d 1939 (CA FC 2004) "we have recognized that the written description requirement can in some cases be satisfied by functional description. See, e.g., Enzo, 296 F.3d at 1324 ("It is not correct, however, that all functional descriptions of genetic material fail to meet the written description requirement."). Nonetheless, such functional description can be sufficient only if there is also a structure-function relationship known to those of ordinary skill in the art."

In the presently claimed invention, no specific sequence is required or claimed. All nucleic acids have the structure-function relationship known to those of ordinary skill in the art for use in the present invention.

Further, the drawings provide sketches of the labeled complexes, the brief descriptions of the drawings and the specification provide descriptions of the nucleic acids of the labeled complexes. Support for a nucleic acid as a gene is found at page 7, line 6; as mRNA is found at page 10, line 14; as tRNA is found at page 10, line 14; as rRNA is found at page 10, line 14; a single-stranded nucleic acid obtained by denaturation of a double stranded nucleic acid is found at page 11, line 8, page 21, lines 7-8, page 34, lines 13-14, and at page 16, line 17-20; a nucleic acid obtained by synthesis is found at page 15, lines 15-17; a nucleic acid obtained by using the polymerase chain reaction is found at page 27, lines 9-14, page 28, lines 22-28, and page 42, lines 25-28; a nucleic acid sequence having a recognition sequence of a restriction enzyme at one end is found at page 28, lines 23-24; a nucleic acid generated by annealing is found at page 15, line 19; and a nucleic acid generated by DNA ligase is found at page 16, line 11, and at page 29, lines 5-6.

Further the claimed length of target receptor is clearly set forth in the specification at page 8, line 28, to page 9, line 9, specifically at line 9. Said lines state:

> *..., the target receptor, ..., is formed in a slender shape ... . (page 9, line 3). The size of the "slender shape" is not expressly defined (page 9, line 5). ... For example, the form is as long as or sufficiently longer than the particle size (page 9, lines 7-8), for example, about 10 times as long as the particle size, for example, about 10μm (page 9, lines 8-9).*

The examiner has converted the 10 micron length to numbers of nucleotides and then rejected the application for lacking a written description of that number of nucleotides. Applicants believe this rejection is improper. There is clear written description for the length of the target receptor.

Further, paragraph 33 of page 12 of the Office Action cites O'Neill *et al.* as meeting a limitation of the length of immobilized nucleic acids up to tens of thousands of nucleotides long since O'Neill *et al.* disclose primer extension reactions and chain terminated sequencing reaction products. Please note that the present application also cites the polymerase chain reaction method using primers and polymerase, and that chain terminated sequencing reactions use primers and polymerase with a dideoxynucleotide that

stops the polymerase. Therefore, Applicants submit that if O'Neill meets the length limitation by such a description, then the present specification also meets the length limitation by such a description.

The *Lockwood* standard of providing words, figures, and diagrams in the specification to provide a written description of the claimed invention is clearly met. Applicants submit that adequate written description is provided by the application as originally filed since nucleic acids are part of the invention in a generic form, not in a sequence specific form.

Applicants respectfully request that the rejection of the claims for lack of adequate written description be withdrawn.

Since the independent claims are supported by the written description of the specification as filed, claims dependent thereon also have support. Applicants respectfully request that the rejection of Claims 8-11 and 35-37 under 35 U.S.C. §112, first paragraph, be withdrawn for the reasons cited herein.

C. Rejections of Claims 8-11 and 35-37 under 35 U.S.C. §112, Second Paragraph

Office Action

Claims 8-11 and 35-37 were rejected as being indefinite for the term "major" and for lacking how one obtains a predetermined base sequence or a predetermined molar ratio of nucleic acids when simply denaturing double stranded nucleic acids.

Response

The claims have been amended to remove the terms "major" and "predetermined base sequence." Further, the predetermined molar ratio is of the types of labeled substances, as distinguished from predetermined molar ratio of nucleic acids. Since the independent claims are now definite, claims dependent thereon also are considered definite. Applicants respectfully request that the rejection of Claims 8-11 and 35-37 under 35 U.S.C. §112, second paragraph, be withdrawn for the reasons cited herein.

D. Common Ownership of the Subject Matter of the Claims

The subject matter of the claims was commonly owned at the time any inventions covered therein were made.

E. Rejections of Claims 8-11 and 35-37 under 35 U.S.C. 102(a and e) as anticipated by or under 35 U.S.C. 103(a) as obvious over U.S. 6,124,092 (O'Neill *et al.*)

Office Action

The Office Action states that Claims 8-11 and 35-37 are rejected over O'Neill *et.al.*. since O'Neill *et.al.* disclose the immobilization of "recovery primers" and "recovery tags," provide a listing of

various solid supports to which one or more nucleic acids are bound, teach that nucleic acids can be labeled with any variety of labels, teach that in one embodiment the nucleic acid can be of from 18-36 nucleotides long, disclose primer extension reactions, and that the predetermined molar ratio is satisfied by PCR and sequencing assays which require the usage of known concentrations of reactants.

Response

The PTO provides in MPEP §2131 that:

"[t]o anticipate a claim, the reference must teach every element of the claim."

Therefore, to support this rejection with respect to each of Claims 35, 36 and 37, the O'Neill *et al.* patent must contain all of the above-claimed elements of each of the claims.

35 U.S.C. §103(a) provides that:

"[a] patent may not be obtained ... if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains ... (emphasis added)"

Thus, when evaluating a claim for determining obviousness, all limitations of the claim must be evaluated.

Independent Claim 35 is not anticipated or rendered obvious by O'Neill *et al.* since O'Neill *et al.* lack teaching or suggestion of:

wherein said target receptors are single-stranded nucleic acids,

wherein the first end of each receptor is bonded with said carrier particle

and

at least a first type and a second type of labeled substance, each labeled substance bonded to a fraction of the number of target receptors at the second end of each receptor.

Please note that when O'Neill *et al.* teach at least a first type and a second type of labeled substance, the target receptor is no longer a single-stranded nucleic acid but is double-stranded. Therefore, O'Neill *et al.* do not teach or suggest the subject matter claimed in Claim 35.

As a result, the rejection based on 35 U.S.C. §102(b) cannot be supported by the O'Neill *et al.* patent as applied to Claim 35. Further, it is impossible to render the subject matter of Claim 35 as a whole obvious based on O'Neill *et al.*, and the above explicit terms of the statute cannot be met. As a result, the examiner's burden of factually supporting a prima facie case of obviousness clearly cannot be met with respect to Claim 35, and a rejection under 35 U.S.C. §103(a) is not applicable.

Independent Claim 36 is not anticipated or rendered obvious by O'Neill *et al.* since O'Neill *et al.* lack teaching or suggestion of:

wherein said target receptors are double stranded nucleic acids, each double stranded nucleic acid having a first single strand and a second single strand, each single strand having a first and a second end, wherein the target receptor has a first end of a first single strand bonded with said carrier;

at least a first type and a second type of labeled substance, each labeled substance bonded to a fraction of the number of target receptors at the second end of a second single strand, thereby forming a labeled complex having a predetermined molar ratio of the types of labeled substances, in all of said labeled substances of the carrier particle.

Please note that when the primer of O'Neill *et al.* is labeled, the first strand is bonded to the carrier and the first strand is bonded to the label. Therefore, O'Neill *et al.* do not teach or suggest the subject matter of Claim 36 when the label is on the primer.

Please note that when the label is on the chain terminator of O'Neill *et al.*, a labeled complex having a predetermined molar ratio of the types of labeled substances is not formed since the molar ratio of labeled substances cannot be predetermined. The molar ratio that forms depends upon the nucleotide sequence and is not predetermined.

As a result, the rejection based on 35 U.S.C. §102(b) cannot be supported by the O'Neill *et al.* patent as applied to Claim 36. Further, it is impossible to render the subject matter of Claim 36 as a whole obvious based on O'Neill *et al.*, and the above explicit terms of the statute cannot be met. As a result, the examiner's burden of factually supporting a prima facie case of obviousness clearly cannot be met with respect to Claim 36, and a rejection under 35 U.S.C. §103(a) is not applicable.

Independent Claim 37 is not anticipated or rendered obvious by O'Neill *et al.* since O'Neill *et al.* lack teaching or suggestion of:

at least a first type and a second type of labeled substance, each labeled substance bonded to a fraction of the number of target receptors at the first end of a first single strand, thereby forming a labeled complex having a predetermined molar ratio of the types of labeled substances in all of said labeled substances of the carrier particle.

Please note that O'Neill *et al.* at column 13, lines 17-23, state: "Binding between the recovery tags and their cognate recovery tag binding compounds does not require the binding of 100% (or even a substantial portion) of the labeled polynucleotides in order to be effective for purposes of the invention. The quantity of polynucleotide bound need only be sufficient to produce a detectable signal from the label on the polynucleotides released in subsequent steps."

Therefore, when the primer of O'Neill *et al.* is labeled, the first strand is bonded to the carrier and the first strand is bonded to the label. In that case, O'Neill *et al.* do not teach a predetermined molar ratio of the types of labeled substances since the amount of polynucleotide bound to form a double stranded target receptor need only produce a detectable signal. O'Neill *et al.* teach a qualitative measure, not a quantitative measure of a predetermined molar ratio of types of labeled substances in all of said labeled substances of the carrier particle.

As a result, the rejection based on 35 U.S.C. §102(b) cannot be supported by the O'Neill *et al.* patent as applied to Claim 37. Further, it is impossible to render the subject matter of Claim 37 as a whole obvious based on O'Neill *et al.*, and the above explicit terms of the statute cannot be met. As a result, the examiner's burden of factually supporting a prima facie case of obviousness clearly cannot be met with respect to Claim 37, and a rejection under 35 U.S.C. §103(a) is not applicable.

Dependent Claims 8-11 depend from, and further limit, independent Claims 35-37 in a patentable sense and therefore are allowable as well. In view of all of the above, the allowance of Claims 8-11 and 35-37 is respectfully requested.

F. Conclusion

It is believed that all matters set forth in the Office Action have been addressed. Further reconsideration and an early indication of the allowability of the pending claims are respectfully requested. Should the Examiner believe that an interview with Applicant's undersigned agent would expedite consideration of the pending claims, the Examiner is invited to call the undersigned agent at 512.867.8528.

Respectfully submitted,

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